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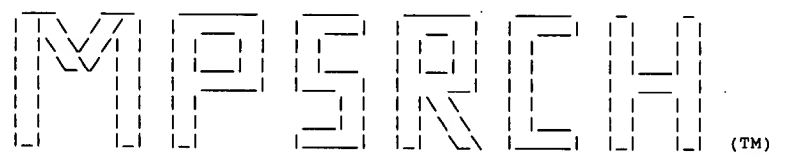

Release 3.1A John F. Collins, Biocomputing Research Unit.

MPsrch_pp protein - protein database search, using Smith-Waterman algorithm

Run on: Mon Oct 2 09:33:11 2000; MasPar time 6.68 Seconds
436.063 Million cell updates/sec

Tabular output not generated.

Title: >US-09-381-497-2
Description: (1-123) from US09381497.pep
Perfect Score: 903
Sequence: 1 EVQLVESGGGLVKPGGSLKL.....SSYGVLFAYWGQGTLVTVSA 123

Scoring table: PAM 150
Gap 11

Searched: 188963 seqs, 23686106 residues

Post-processing: Minimum Match 0%
Listing first 45 summaries

Database: a-geneseq36
1:geneseqp

Statistics: Mean 30.324; Variance 152.652; scale 0.199

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description	Pred. No.
1	896	99.2	123	1	W66099	anti-CD22 monoclonal a	1.58e-63
2	748	82.8	121	1	W86125	Protein sequence of mo	3.76e-51
3	744	82.4	121	1	W22951	Monoclonal antibody (M	8.11e-51
4	744	82.4	121	1	W86118	Murine 340 Vh amino ac	8.11e-51
5	735	81.4	139	1	W21656	Chimeric MAb 15 PCR-mo	4.56e-50
6	730	80.8	140	1	W21654	Mouse MAb 15 heavy cha	1.19e-49
7	728	80.6	136	1	R06251	Variable region of mur	1.75e-49
8	717	79.4	139	1	R52773	Murine KC-4 immunoglob	1.44e-48
9	717	79.4	139	1	R52791	Murine KC-4 immunoglob	1.44e-48
10	716	79.3	118	1	W89627	Mouse humanised antibo	1.74e-48
11	716	79.3	118	1	W57576	Chimeric H chain SEQ I	1.74e-48
12	716	79.3	137	1	W89625	Mouse humanised antibo	1.74e-48
13	716	79.3	137	1	W57592	Chimeric antibody agai	1.74e-48
14	716	79.3	247	1	W11917	Murine MAb SK48-E26 he	1.74e-48
15	713	79.0	121	1	W86122	Protein sequence of de	3.10e-48
16	713	79.0	123	1	W08582	Human antibody C4.1 he	3.10e-48
17	712	78.8	121	1	W86120	Protein sequence of hu	3.75e-48
18	712	78.8	139	1	W21652	Humanised reshaped MAb	3.75e-48
19	710	78.6	138	1	R20064	MRK16-H chain.	5.50e-48
20	709	78.5	117	1	W76003	LM609 antibody heavy c	6.67e-48
21	706	78.2	142	1	R30882	Antibody 4A2 heavy cha	1.18e-47
22	704	78.0	138	1	W03722	Anti-human gp39 MAb 39	1.74e-47
23	703	77.9	123	1	R43827	Anti-lysozyme VH.	2.10e-47
24	703	77.9	123	1	R45187	Heavy chain variable d	2.10e-47
25	700	77.5	119	1	W73503	Antibody 15D3 heavy ch	3.74e-47
26	700	77.5	119	1	W69322	15D3 antibody heavy ch	3.74e-47
27	700	77.5	158	1	W19577	Mouse anti-idiotypic a	3.74e-47
28	700	77.5	158	1	W19579	Mouse anti-idiotypic a	3.74e-47
29	698	77.3	119	1	W29996	Humanised variant of h	5.48e-47
30	697	77.2	120	1	W00240	EGF receptor chimeric	6.64e-47
31	696	77.1	117	1	R79155	Human IgE receptor-bin	8.04e-47
32	696	77.1	117	1	W27354	Heavy chain variable r	8.04e-47
33	696	77.1	117	1	W27357	Heavy chain variable r	8.04e-47
34	693	76.7	121	1	W86124	Protein sequence of al	1.43e-46
35	692	76.6	118	1	R41233	Monoclonal antibody BW	1.73e-46
36	692	76.6	119	1	R56239	VH region of anti-fuco	1.73e-46
37	692	76.6	138	1	R32246	BR55-2 murine IgG3 hea	1.73e-46
38	692	76.6	138	1	R32242	Chimeric MAb heavy cha	1.73e-46
39	692	76.6	139	1	R31588	BR55-2 heavy chain var	1.73e-46
40	691	76.5	119	1	W29994	Heavy chain variable r	2.09e-46
41	691	76.5	140	1	W06205	Xenograft antibody HAR	2.09e-46
42	689	76.3	448	1	R97376	Murine anti-BGH MAb he	3.07e-46
43	687	76.1	448	1	R43673	Mouse anti-bovine grow	4.50e-46
44	686	76.0	448	1	R06476	Heavy chain of anti-bo	5.45e-46
45	685	75.9	117	1	R79157	Human IgE receptor-bin	6.60e-46

ALIGNMENTS

```
RESULT    1
ID   W66099 standard; Protein; 123 AA.
AC   W66099;
DT   10-DEC-1998  (first entry)
DE   anti-CD22 monoclonal antibody heavy chain variable region.
KW   anti-CD22 monoclonal antibody heavy chain variable region; VL;
KW   Pseudomonas exotoxin; variable heavy chain; VH; variable light chain;
KW   malignant B-cell; immunodiagnosis; RFB4 IgG.
OS   Mammalia.
FH   Key             Location/Qualifiers
FT   Misc_difference 121
FT                   /note= "Encoded by gtc"
PN   WO9841641-A1.
PD   24-SEP-1998.
PF   19-MAR-1998; U05453.
PR   20-MAR-1997; US-041437.
PA   (USSH ) US DEPT HEALTH & HUMAN SERVICES.
PI   Fitzgerald D, Kreitman R, Mansfield E, Pastan I;
DR   WPI; 98-521227/44.
DR   N-PSDB; V07642.
PT   Recombinant anti-CD22 antibodies and immuno-conjugates - of
PT   antibodies linked to a therapeutic agent, e.g. Pseudomonas exotoxin
PT   or a label; for inhibiting malignant B-cells
PS   Claim 6; Fig 1; 71pp; English.
CC   The invention claims for a recombinant immunoconjugate comprising
CC   of a therapeutic agent (e.g Pseudomonas exotoxin) or a detectable
CC   label peptide bonded to a recombinant anti-CD22 antibody (RFB4 IgG)
CC   having the present variable heavy (VH) chain with a cysteine residue
CC   at amino acid 44 and a variable light (VL; W66098) chain with a
CC   cysteine residue at amino acid 100.  The immunoconjugate is claimed
CC   to inhibit the growth of malignant B-cells in vivo, such as rodent,
CC   canine or primate B-cells.  The anti-CD22 antibody is claimed useful
CC   for detecting CD22 protein in a sample or in vivo in a mammal, and
CC   can be used in diagnostic kits.
SQ   Sequence   123 AA;

  Query Match           99.2%;  Score 896;  DB 1;  Length 123;
  Best Local Similarity  99.2%;  Pred. No. 1.58e-63;
  Matches   122;  Conservative    0;  Mismatches   1;  Indels   0;  Gaps   0;

Db       1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy       1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60

Db      61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAYWGQGTLVT 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Qy      61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAYWGQGTLVT 120
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Db    121 TSA 123
          ||
Qy    121 VSA 123


RESULT    2
ID   W86125 standard; Protein; 121 AA.
AC   W86125;
DT   03-MAR-1999  (first entry)
DE   Protein sequence of mouse de-immunised 340 Vh.
KW   Non-immunogenic; epitope; T-cell; immunogenicity; immune system; SK;
KW   immunoglobulin; therapeutic; streptokinase; de-immunised; murine.
OS   Mus sp.
PN   WO9852976-A1.
PD   26-NOV-1998.
PF   21-MAY-1998; G01473.
PR   14-APR-1998; GB-007751.
PR   21-MAY-1997; GB-010480.
PR   31-JUL-1997; GB-016197.
PR   28-NOV-1997; GB-025270.
PR   02-DEC-1997; US-067235.
PA   (BIOV-) BIOVATION LTD.
PI   Carr FJ;
DR   WPI; 99-045301/04.
PT   Reducing immunogenicity of proteins - by modifying the amino acid
PT   sequence of the protein to eliminate potential epitopes for T-cells
PT   of a given species
PS   Example 2; Fig 10; 77pp; English.
CC   The invention relates to a method for the production of non-immunogenic
CC   proteins. The method comprises determining at least part of the amino
CC   acid sequence of the protein; (b) identifying in the amino acid sequence
CC   one or more potential epitopes for T-cells (T-cell epitopes) of the given
CC   species; and (c) modifying the amino acid sequence to eliminate at least
CC   one of the T-cell epitopes identified in step (b) thereby to eliminate or
CC   reduce the immunogenicity of the protein when exposed to the immune
CC   system of the given species. A method of analysing a pre-existing protein
CC   to predict the basis for immunogenic responses is also provided. The
CC   methods can be used particularly for reducing the immunogenicity of
CC   immunoglobulins or therapeutic proteins, e.g. Streptokinase (SK). The
CC   products can be used for diagnosis and therapy. The present sequence
CC   represents the protein sequence of mouse de-immunised 340 Vh.
SQ   Sequence   121 AA;

  Query Match           82.8%;  Score 748;  DB 1;  Length 121;
  Best Local Similarity  83.7%;  Pred. No. 3.76e-51;
  Matches   103;  Conservative    7;  Mismatches  11;  Indels    2;  Gaps    1;

Db      1 EVQLVESGGGLVKAGGSLKLSCAASGFAFDTYDMSWVRQTPEKRLEWVAYIGSGGDRTYY 60
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Qy      1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60

Db     61 PDTVKGRFTISRDNGKNSLYLQMNSLKSEDTAMYYCARHYGHYVDYAV--DYWGQGTSVT 118
          |||||||||||||:||:|||||:|||||||||||||||| |    |:|   |||||| ||
Qy     61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAYWGQGTLVT 120

Db    119 VSS 121
          ||:
Qy    121 VSA 123


RESULT    3
ID   W22951 standard; Protein; 121 AA.
AC   W22951;
DT   02-APR-1998  (first entry)
DE   Monoclonal antibody (MAb) 340 heavy chain variable region.
KW   MAb 340; monoclonal antibody; foetal cell; pre-natal diagnosis;
KW   erythrocyte; trophoblast; genetic abnormality; foetal sex; analysis;
KW   epidermal growth factor receptor; EGFr; Down's syndrome; human.
OS   Mus sp.
FH   Key             Location/Qualifiers
FT   Region          1. .30
FT                   /note= "Framework 1"
FT   Region          31. .35
FT                   /note= "Complementarity-determining region 1"
FT   Region          36. .55
FT                   /note= "Framework 2"
FT   Region          56. .66
FT                   /note= "Complementarity-determining region 2"
FT   Region          67. .98
FT                   /note= "Framework 3"
FT   Region          97. .110
FT                   /note= "Complementarity-determining region 3"
FT   Region          111. .121
FT                   /note= "Framework 4"
PN   WO9730354-A2.
PD   21-AUG-1997.
PF   17-FEB-1997; G00443.
PR   16-FEB-1996; GB-003249.
PA   (UYNO-) UNIV NOTTINGHAM.
PI   Durrant LG, Liu DT;
DR   WPI; 97-425169/39.
DR   N-PSDB; T75583.
PT   Foetal cell analysis comprising isolating at least 2 sorts of foetal
PT   cell from maternal sample - specifically nucleated red cells and
PT   trophoblasts, useful for pre-natal diagnosis of genetic
PT   abnormalities or foetal sex
PS   Example 2; Page 15; 31pp; English.
CC   This is the heavy chain variable region of a monoclonal antibody (MAb)
CC   340. The MAb 340 acts as a trophoblast binding agent in a method for
CC   analysing human foetal cells. The method comprises isolating at least 2
CC   types of nucleated foetal cell from a maternal sample. The foetal cells
CC   specifically are nucleated red cells (erythrocytes) and trophoblasts.
CC   The trophoblasts are isolated by contacting the maternal sample with a
CC   specific binding agent that binds to the epidermal growth factor receptor
CC   (EGFr). MAb340 or an EGFr binding derivative of MAb340 comprising at
CC   least the CDR regions of one or other of the light or heavy chain
CC   variable regions of MAb 340 is used as the binding agent. Erythrocytes
CC   are also isolated with a specific anti-transferrin antibody. The target
CC   nucleotide sequences in the foetal cells are amplified by PCR primers.
CC   The isolated cells can be used for genetic and biochemical analysis,
CC   particularly to determine the sex of the foetus or to detect inherited
CC   abnormalities, e.g. Down's syndrome. More generally MAb 340 can be used
CC   to enrich (for subsequent analysis) rare malignant cells, e.g. squamous
CC   carcinoma cells, that express EGF receptor. The method is not
CC   significantly invasive and does not carry the risk of inducing abortion.
CC   Use of two types of cells significantly improves the sensitivity of
CC   pre-natal diagnosis.
SQ   Sequence   121 AA;

  Query Match           82.4%;  Score 744;  DB 1;  Length 121;
  Best Local Similarity  83.7%;  Pred. No. 8.11e-51;
  Matches   103;  Conservative    7;  Mismatches  11;  Indels    2;  Gaps    1;

Db      1 EVQLVESGGGLVKAGGSLKLSCAASGFAFDTYDMSWVRQTPEKRLEWVAYIGSGGDRTYY 60
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Qy      1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60

Db     61 PDTVKGRFTISRDNGKNTLYLQLNSLKSEDTAMYYCARHYGHYVDYAV--DYWGQGTSVT 118
          |||||||||||||:|||||||::|||||||||||||||| |    |:|   |||||| ||
Qy     61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAYWGQGTLVT 120

Db    119 VSS 121
          ||:
Qy    121 VSA 123


RESULT    4
ID   W86118 standard; Protein; 121 AA.
AC   W86118;
DT   03-MAR-1999  (first entry)
DE   Murine 340 Vh amino acid sequence.
KW   Non-immunogenic; epitope; T-cell; immunogenicity; immune system; SK;
KW   immunoglobulin; therapeutic; streptokinase; diagnosis; murine.
OS   Mus sp.
PN   WO9852976-A1.
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PD   26-NOV-1998.
PF   21-MAY-1998; G01473.
PR   14-APR-1998; GB-007751.
PR   21-MAY-1997; GB-010480.
PR   31-JUL-1997; GB-016197.
PR   28-NOV-1997; GB-025270.
PR   02-DEC-1997; US-067235.
PA   (BIOV-) BIOVATION LTD.
PI   Carr FJ;
DR   WPI; 99-045301/04.
DR   N-PSDB; V81002.
PT   Reducing immunogenicity of proteins - by modifying the amino acid
PT   sequence of the protein to eliminate potential epitopes for T-cells
PT   of a given species
PS   Example 1; Fig 2; 77pp; English.
CC   The invention relates to a method for the production of non-immunogenic
CC   proteins. The method comprises determining at least part of the amino
CC   acid sequence of the protein; (b) identifying in the amino acid sequence
CC   one or more potential epitopes for T-cells (T-cell epitopes) of the given
CC   species; and (c) modifying the amino acid sequence to eliminate at least
CC   one of the T-cell epitopes identified in step (b) thereby to eliminate or
CC   reduce the immunogenicity of the protein when exposed to the immune
CC   system of the given species. A method of analysing a pre-existing protein
CC   to predict the basis for immunogenic responses is also provided. The
CC   methods can be used particularly for reducing the immunogenicity of
CC   immunoglobulins or therapeutic proteins, e.g. Streptokinase (SK). The
CC   products can be used for diagnosis and therapy. The present sequence
CC   represents the amino acid sequence of murine 340 Vh.
SQ   Sequence   121 AA;

  Query Match           82.4%;  Score 744;  DB 1;  Length 121;
  Best Local Similarity  83.7%;  Pred. No. 8.11e-51;
  Matches   103;  Conservative    7;  Mismatches  11;  Indels   2;  Gaps   1;

Db       1 EVQLVESGGGLVKAGGSLKLSCAASGFAFDTYDMSWVRQTPEKRLEWVAYIGSGGDRTYY 60
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Qy       1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60

Db      61 PDTVKGRFTISRDNGKNTLYLQLNSLKSEDTAMYYCARHYGHYVDYAV--DYWGQGTSVT 118
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Qy      61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAYWGQGTLVT 120

Db     119 VSS 121
           |||
Qy     121 VSA 123


RESULT    5
ID   W21656 standard; Protein; 139 AA.
AC   W21656;
DT   03-JAN-1998  (first entry)
DE   Chimeric MAb 15 PCR-modified heavy chain variable region.
KW   Humanised antibody; monoclonal antibody; MAb 15; tumour;
KW   lung cancer; therapy.
OS   Chimeric Mus musculus.
OS   Chimeric synthetic.
FH   Key             Location/Qualifiers
FT   Peptide         1. .19
FT                   /label= Sig_peptide
FT   Protein         25. .139
FT                   /label= Mat_protein
FT   Region          20. .49
FT                   /label= Framework-1
FT   Region          50. .54
FT                   /label= CDR1
FT                   /note= "complementarity determining region 1"
FT   Region          55. .68
FT                   /label= Framework-2
FT   Region          69. .86
FT                   /label= CDR2
FT                   /note= "complementarity determining region 2"
FT   Region          87. .117
FT                   /label= Framework-3
FT   Region          118. .128
FT                   /label= CDR3
FT                   /note= "complementarity determining region 3"
FT   Region          129. .138
FT                   /label= Framework-4
PN   EP-781847-A1.
PD   02-JUL-1997.
PF   25-OCT-1996; 117154.
PR   06-NOV-1995; EP-117407.
PA   (MERE ) MERCK PATENT GMBH.
PI   Bendig M,  Jones T,  Saldana J;
DR   WPI; 97-334904/31.
DR   N-PSDB; T72269.
PT   Humanised form of murine monoclonal antibody MAb 15 - useful for
PT   treating lung cancer
PS   Disclosure; Fig 5; 71pp; English.
CC   This polypeptide comprises the heavy chain variable region VH
CC   region of murine monoclonal antibody (MAb) 15 (DSM ACC2117).  It is
CC   encoded by a MAb 15 VH cDNA sequence (T72269) modified for the
CC   expression of chimeric antibody.  The VL sequence was similarly
CC   obtained (see W21655).  The modified VH and VL sequences were used
CC   in a claimed process to model and design novel humanised, reshaped
CC   MAb 15 having humanised, reshaped VH and VL sequences (see W21652
CC   and W21651), which can be used for treating tumours, especially
CC   lung cancer, and for the manufacture of a drug related to tumours,
CC   especially lung cancer.
SQ   Sequence   139 AA;

  Query Match           81.4%;  Score 735;  DB 1;  Length 139;
  Best Local Similarity  82.9%;  Pred. No. 4.56e-50;
  Matches   102;  Conservative    9;  Mismatches   9;  Indels   3;  Gaps   1;

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Qy       1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60

Db      80 PDTVKGRFTISRDNAKKILFLQMTSLKSEDAAMYYCARHGEEVRPW---FDYWGQGTLVT 136
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Qy      61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAYWGQGTLVT 120

Db     137 VSA 139
           |||
Qy     121 VSA 123


RESULT    6
ID   W21654 standard; Protein; 140 AA.
AC   W21654;
DT   03-JAN-1998  (first entry)
DE   Mouse MAb 15 heavy chain variable region.
KW   Humanised antibody; monoclonal antibody; MAb 15; tumour;
KW   lung cancer; therapy.
OS   Mus musculus.
FH   Key             Location/Qualifiers
FT   Peptide         1. .19
FT                   /label= Sig_peptide
FT   Protein         20. .140
FT                   /label= Mat_protein
FT   Region          20. .49
FT                   /label= Framework-1
FT   Region          50. .53
FT                   /label= CDR1
FT                   /note= "complementarity determining region 1"
FT   Region          54. .68
FT                   /label= Framework-2
FT   Region          69. .86
FT                   /label= CDR2
FT                   /note= "complementarity determining region 2"
FT   Region          87. .117
FT                   /label= Framework-3
FT   Region          118. .128
FT                   /label= CDR3
FT                   /note= "complementarity determining region 3"
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FT   Region          129. .139
FT                   /label= Framework-4
PN   EP-781847-A1.
PD   02-JUL-1997.
PF   25-OCT-1996; 117154.
PR   06-NOV-1995; EP-117407.
PA   (MERE ) MERCK PATENT GMBH.
PI   Bendig M,  Jones T,  Saldana J;
DR   WPI; 97-334904/31.
DR   N-PSDB; T72267.
PT   Humanised form of murine monoclonal antibody MAb 15 - useful for
PT   treating lung cancer
PS   Example 1; Fig 2; 71pp; English.
CC   This polypeptide comprises the heavy chain variable region VH
CC   of murine monoclonal antibody (MAb) 15 (DSM ACC2117), a MAb that
CC   shows a therapeutic effect on human tumour cells, especially human
CC   lung cancer.  Its sequence was deduced from an isolated cDNA
CC   cloner (see T72267).  The MAb 15 VL region sequence (W21653)
CC   has also been determined.  Amplified VH and VL cDNA sequences were
CC   used in a claimed process for the production of novel humanised,
CC   reshaped MAb 15 having humanised, reshaped VH and VL regions (see
CC   W21652 and W21651), which can be used for treating tumours,
CC   especially lung cancer, and for the manufacture of a drug related
CC   to tumours, especially lung cancer.
SQ   Sequence   140 AA;

  Query Match           80.8%;  Score 730;  DB 1;  Length 140;
  Best Local Similarity  82.1%;  Pred. No. 1.19e-49;
  Matches   101;  Conservative   10;  Mismatches   9;  Indels   3;  Gaps   1;

Db     20 EVQVVESGGGLVKPGGSLKLSCAASGFAFSDYDMSWVRQTPEKKLEWVAYLSRGGGSTYY 79
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Qy      1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60

Db     80 PDTVKGRFTISRDNAKKILFLQMTSLKSEDAAMYYCARHGEEVRPW---FDYWGQGTLVT 136
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Qy     61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAYWGQGTLVT 120

Db    137 VSA 139
          |||
Qy    121 VSA 123


RESULT    7
ID   R06251 standard; protein; 136 AA.
AC   R06251;
DT   10-DEC-1990 (first entry)
DE   Variable region of murine AHT 54 heavy chain.
KW   Interleukin-2 receptor; IL-2; tumour necrosis factor; TNF; ss.
OS   Mus sp.
PN   EP-380068-A.
PD   01-AUG-1990.
PF   24-JAN-1990; 101351.
PR   24-JAN-1989; US-301216.
PR   04-DEC-1989; US-441702.
PA   (MOLE-) MOLECULAR THERAPEU.
PI   Zerler B;
DR   WPI; 90-232892/31.
DR   N-PSDB; Q05555.
PT   Expression vectors for producing chimeric monoclonal antibodies -
PT   which express human constant region and non-human variable region
PS   Disclosure; p; English.
CC   MAbs comprising mouse CH and CL constant regions whith human
CC   variable regions may be used to create mouse/human hybrid MAbs,
CC   which have a longer serum half-life. Method can be used to produce
CC   Abs against interleukin-2 receptor and tumour necrosis factor.
SQ   Sequence   136 AA;

  Query Match           80.6%;  Score 728;  DB 1;  Length 136;
  Best Local Similarity  88.6%;  Pred. No. 1.75e-49;
  Matches   109;  Conservative    3;  Mismatches   5;  Indels   6;  Gaps   1;

Db     20 EVQLVESGGGLVKPGGSLKLSCAASGFAFSSIDMSWVRQTPEKRLEWVAYISSGGDNTYY 79
          |||||||||||||||||||||||||| |||||||||||||||||||| |||
Qy      1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60

Db     80 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAVYYCARR------YGLPFAYWGQGTLVT 133
          |||||||||||||||||||||||||||||:|||||:      ||: ||||||||||
Qy     61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAYWGQGTLVT 120

Db    134 VSA 136
          |||
Qy    121 VSA 123


RESULT    8
ID   R52773 standard; Protein; 139 AA.
AC   R52773;
DT   24-JAN-1995  (first entry)
DE   Murine KC-4 immunoglobulin heavy chain variable region (deduced).
KW   Immunoglobulin variable domain; primer; polymerase chain reaction;
KW   chimeric antibody; human milk fat globule; human breast carcinoma;
KW   murine anti-human carcinoma monoclonal antibody KC-4.
OS   Mus musculus.
FH   Key             Location/Qualifiers
FT   protein         20. .139
FT                   /label= KC-4_mature_VL-chain
FT   region          20. .49
FT                   /label= FR1
FT   region          50. .54
FT                   /label= CDR1
FT   region          55. .68
FT                   /label= FR2
FT   region          69. .85
FT                   /label= CDR2
FT   region          86. .117
FT                   /label= FR3
FT   region          118. .128
FT                   /label= CDR3
FT   region          129. .139
FT                   /label= FR4
PN   WO9411508-A.
PD   26-MAY-1994.
PF   15-NOV-1993; U11316.
PR   13-NOV-1992; US-977706.
PR   13-NOV-1992; US-977707.
PR   28-SEP-1993; US-128015.
PA   (CANC-) CANCER RES FUND CONTRA COSTA.
DR   WPI; 94-183509/22.
DR   N-PSDB; Q62764.
PT   Chimeric human-murine polypeptide(s) specific for human mammary
PT   fat globule antigen - for imaging, diagnosing and treating
PT   neoplasia, with less undesirable immunogenic response
PS   Example 27; Page 41; 54pp; English.
CC   An initial isolation of cDNAs coding for murine anti-human breast
CC   carcinoma MAb KC-4 was performed using PCR with commercially
CC   available primers (see Q62751-Q62758, available from NOVAGEN).
CC   Subsequent cloning using PCR primers JO20, JO21, JO22 and JO24
CC   (see Q62759-Q62762) resulted in the isolation of the mouse Ig
CC   variable domains. The amplified cDNAs were sequenced (Q62763 and
CC   Q62764) and amino acid sequences were deduced from them. Chimeric
CC   mouse-human antibodies were constructed using human constant
CC   regions so as to produce less immunogenic polypeptides which
CC   retained the anti-human carcinoma binding specificity of KC-4.
SQ   Sequence   139 AA;

  Query Match           79.4%;  Score 717;  DB 1;  Length 139;
  Best Local Similarity  82.1%;  Pred. No. 1.44e-48;
  Matches   101;  Conservative    8;  Mismatches  11;  Indels   3;  Gaps   3;

Db     20 EVQMVESGGGLVKPGGSLKLSCAASGFAFSSYAMSWVRQSPEKRLEWVAEISSGGNYAYY 79
          |||:|||||||||||||||||||||||| | ||||||:||||||||| |||||  :||
Qy      1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60

Db     80 QDTVTGRFTISRDNAKNTLYLEMSSLRSEDTAMYYCARED-YGIP-A-WFAYWGQGTLVS 136
          ||| ||||||||||||||||:||||:||||||||||   || : :  ||||||||||:
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Qy      61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAYWGQGTLVT 120

Db     137 VSA 139
           |||
Qy     121 VSA 123


RESULT    9
ID    R52791 standard; Protein; 139 AA.
AC    R52791;
DT    24-JAN-1995  (first entry)
DE    Murine KC-4 immunoglobulin heavy chain variable region (deduced).
KW    Immunoglobulin variable domain; primer; polymerase chain reaction;
KW    chimeric antibody; human milk fat globule; human breast carcinoma;
KW    murine anti-human carcinoma monoclonal antibody KC-4.
OS    Mus musculus.
FH    Key             Location/Qualifiers
FT    protein         20. .139
FT                    /label= KC-4_mature_VL-chain
FT    region          20. .49
FT                    /label= FR1
FT    region          50. .54
FT                    /label= CDR1
FT    region          55. .68
FT                    /label= FR2
FT    region          69. .85
FT                    /label= CDR2
FT    region          86. .117
FT                    /label= FR3
FT    region          118. .128
FT                    /label= CDR3
FT    region          129. .139
FT                    /label= FR4
PN    WO9411509-A.
PD    26-MAY-1994.
PF    16-NOV-1993; U11445.
PR    16-NOV-1992; US-977696.
PR    30-SEP-1993; US-129930.
PR    08-OCT-1993; US-134346.
PA    (CANC-) CANCER RES FUND CONTRA COSTA.
PI    Ceriani RL,  Do Couto FJR,  Padlan EA,  Peterson JA;
DR    WPI; 94-183510/22.
PT    New analogue peptide(s) comprising antibody variable regions -
PT    used to develop prods. for use in the detection, diagnosis,
PT    therapy and prevention of neoplasms
PS    Example 26; Page 61; 109pp; English.
CC    An initial isolation of cDNAs coding for murine anti-human breast
CC    carcinoma MAb KC-4 was performed using PCR with commercially
CC    available primers (see Q62776-Q62783, available from NOVAGEN).
CC    Subsequent cloning using PCR primers JO20, JO21, JO22 and JO24
CC    (see Q62784-Q62787) resulted in the isolation of the mouse Ig
CC    variable domains. The amplified cDNAs were sequenced (Q62788 and
CC    Q62789) and amino acid sequences were deduced from them. Chimeric
CC    mouse-human antibodies were constructed using human constant
CC    regions so as to produce less immunogenic polypeptides which
CC    retained the anti-human carcinoma binding specificity of KC-4.
SQ    Sequence   139 AA;

  Query Match           79.4%;  Score 717;  DB 1;  Length 139;
  Best Local Similarity  82.1%;  Pred. No. 1.44e-48;
  Matches   101;  Conservative    8;  Mismatches  11;  Indels   3;  Gaps   3;

Db      20 EVQMVESGGGLVKPGGSLKLSCAASGFAFSSYAMSWVRQSPEKRLEWVAEISSGGNYAYY 79
           |||:||||||||||||||||||||||||| | ||||||:||||||||| |||||  :||
Qy       1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60

Db      80 QDTVTGRFTISRDNAKNTLYLEMSSLRSEDTAMYYCARED-YGIP-A-WFAYWGQGTLVS 136
           ||| |||||||||||||||:||||:||||||||||||   || : :  ||||||||||:
Qy      61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAYWGQGTLVT 120

Db     137 VSA 139
           |||
Qy     121 VSA 123


RESULT   10
ID    W89627 standard; Protein; 118 AA.
AC    W89627;
DT    14-APR-1999  (first entry)
DE    Mouse humanised antibody #23-57-137-1 heavy chain mature protein.
KW    Human; parathyroid hormone related protein; PTHrP; cachexia; cancer;
KW    inhibitor; humanised.
OS    Mus sp.
OS    Synthetic.
PN    WO9851329-A1.
PD    19-NOV-1998.
PF    13-MAY-1998; J02116.
PR    18-JUL-1997; JP-194445.
PR    15-MAY-1997; JP-125505.
PA    (CHUS ) CHUGAI SEIYAKU KK.
PI    Ishii K, Sato K, Tunenari T;
DR    WPI; 99-070101/06.
PT    Inhibitors of binding of parathyroid hormone related peptide to its
PT    receptor - useful for, e.g. treatment of cachexia arising from
PT    cancer or other diseases
PS    Example 2; Page 72-73; 125pp; Japanese.
CC    The present invention describes compositions for the treatment of
CC    cachexia containing a substance which inhibits the binding of a
CC    parathyroid hormone related peptide (PTHrP) to its receptor, as an
CC    active component. This substance may be an antagonist to the receptor,
CC    or an antibody (preferably monoclonal) or antibody fragment,
CC    recognising PTHrP. The antibody is preferably humanised or chimeric.
CC    The present invention also describes a humanised antibody prepared
CC    by hybridoma 23-57-137-1 (FERM BP-5631). The composition is used for
CC    the treatment of cachexia arising in connection with diseases such as
CC    cancer, thereby improving the quality of life of the patient. The
CC    present sequence represents mouse humanised antibody heavy chain from
CC    #23-57-137-1 from the present invention.
SQ    Sequence   118 AA;

  Query Match           79.3%;  Score 716;  DB 1;  Length 118;
  Best Local Similarity  82.9%;  Pred. No. 1.74e-48;
  Matches   102;  Conservative    9;  Mismatches   7;  Indels   5;  Gaps   2;

Db       1 EVQLVESGGDLVKPGGSLKLSCAASGFTFSSYGMSWIRQTPDKRLEWVATISSGGSYTYY 60
           ||||||||| ||||||||||||||||||:|| | |||:||||:||||||| |||||: |||
Qy       1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60

Db      61 PDSVKGRFTISRDNAKNTLYLQMSSLKSEDTAMFYCARQTT--MTY---FAYWGQGTLVT 115
           ||:||||||||||||||||||||||||||||:||||::    :|   ||||||||||
Qy      61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAYWGQGTLVT 120

Db     116 VSA 118
           |||
Qy     121 VSA 123


RESULT   11
ID    W57576 standard; protein; 118 AA.
AC    W57576;
DT    03-SEP-1998  (first entry)
DE    Chimeric H chain SEQ ID NO:46 for an antibody against hPTRP.
KW    Chimeric; antibody; human parathormone related peptide; hPTRP; mouse;
KW    L chain; H chain; hypercalcaemia; cancer; malignant lymphoma; CDR;
KW    hypophosphaemia; pathogen; vitamin D resistance; V region; C region;
KW    humanised.
OS    Synthetic.
OS    Chimeric - Mus sp.
OS    Chimeric - Homo sapiens.
PN    WO9813388-A1.
PD    02-APR-1998.
PF    24-SEP-1997; J03382.
PR    24-JUL-1997; JP-214168.
PR    26-SEP-1996; JP-255196.
PA    (CHUS ) CHUGAI SEIYAKU KK.
PI    Sato K, Wakahara Y, Yabuta N;
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DR   WPI; 98-230640/20.
PT   New chimeric antibodies against human parathormone related
PT   peptide(s) - useful for, e.g. treatment of hypercalcaemia and other
PT   disorders caused by malignant neoplasm(s)
PS   Claim 5; Page 111-112; 182pp; Japanese.
CC   New antibodies have been developed which are specific for human
CC   parathormone related peptides (hPTRP). The antibodies comprise chimeric
CC   L and/or H chains, where the C region is of human and L region of mouse,
CC   origin. The present sequence represents a specifically claimed region of
CC   an antibody of the invention. Host cells, transformed with vectors
CC   containing DNA encoding antibodies of the invention, can be used to
CC   produce the antibodies. The antibodies may be used to treat
CC   hypercalcaemia, especially that due to a malignancy, e.g. cancers of
CC   pancreas, lung, throat, larynx, tongue, gum, oesophagus, stomach, liver,
CC   breast, kidney, bladder, womb or prostate or malignant lymphoma. They
CC   may also be used for treatment of hypophosphaemia such as that due to
CC   pathogens or to vitamin D resistance.
SQ   Sequence   118 AA;

  Query Match           79.3%;  Score 716;  DB 1;  Length 118;
  Best Local Similarity  82.9%;  Pred. No. 1.74e-48;
  Matches   102;  Conservative    9;  Mismatches   7;  Indels   5;  Gaps   2;

Db       1 EVQLVESGGDLVKPGGSLKLSCAASGFTFSSYGMSWIRQTPDKRLEWVATISSGGSYTYY 60
           ||||||||| |||||||||||||||||:|| | |||:||||:||||||| ||||||: |||
Qy       1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60

Db      61 PDSVKGRFTISRDNAKNTLYLQMSSLKSEDTAMFYCARQTT--MTY---FAYWGQGTLVT 115
           ||:|||||||||||||||||||||||||||||||:||||::    :|   ||||||||||
Qy      61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAYWGQGTLVT 120

Db     116 VSA 118
           |||
Qy     121 VSA 123


RESULT   12
ID   W89625 standard; Protein; 137 AA.
AC   W89625;
DT   14-APR-1999  (first entry)
DE   Mouse humanised antibody #23-57-137-1 heavy chain protein.
KW   Human; parathyroid hormone related protein; PTHrP; cachexia; cancer;
KW   inhibitor; humanised.
OS   Mus sp.
OS   Synthetic.
FH   Key             Location/Qualifiers
FT   Peptide         1. .19
FT                   /label= signal
FT   Protein         20. .137
PN   WO9851329-A1.
PD   19-NOV-1998.
PF   13-MAY-1998; J02116.
PR   18-JUL-1997; JP-194445.
PR   15-MAY-1997; JP-125505.
PA   (CHUS ) CHUGAI SEIYAKU KK.
PI   Ishii K, Sato K, Tunenari T;
DR   WPI; 99-070101/06.
DR   N-PSDB; X00092.
PT   Inhibitors of binding of parathyroid hormone related peptide to its
PT   receptor - useful for, e.g. treatment of cachexia arising from
PT   cancer or other diseases
PS   Example 2; Page 82; 125pp; Japanese.
CC   The present invention describes compositions for the treatment of
CC   cachexia containing a substance which inhibits the binding of a
CC   parathyroid hormone related peptide (PTHrP) to its receptor, as an
CC   active component. This substance may be an antagonist to the receptor,
CC   or an antibody (preferably monoclonal) or antibody fragment,
CC   recognising PTHrP. The antibody is preferably humanised or chimeric.
CC   The present invention also describes a humanised antibody prepared
CC   by hybridoma 23-57-137-1 (FERM BP-5631). The composition is used for
CC   the treatment of cachexia arising in connection with diseases such as
CC   cancer, thereby improving the quality of life of the patient. The
CC   present sequence represents mouse humanised antibody heavy chain from
CC   #23-57-137-1 from the present invention.
SQ   Sequence   137 AA;

  Query Match           79.3%;  Score 716;  DB 1;  Length 137;
  Best Local Similarity  82.9%;  Pred. No. 1.74e-48;
  Matches   102;  Conservative    9;  Mismatches   7;  Indels   5;  Gaps   2;

Db      20 EVQLVESGGDLVKPGGSLKLSCAASGFTFSSYGMSWIRQTPDKRLEWVATISSGGSYTYY 79
           ||||||||| |||||||||||||||||:|| | |||:||||:||||||| ||||||: |||
Qy       1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60

Db      80 PDSVKGRFTISRDNAKNTLYLQMSSLKSEDTAMFYCARQTT--MTY---FAYWGQGTLVT 134
           ||:|||||||||||||||||||||||||||||||:||||::    :|   ||||||||||
Qy      61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAYWGQGTLVT 120

Db     135 VSA 137
           |||
Qy     121 VSA 123


RESULT   13
ID   W57592 standard; protein; 137 AA.
AC   W57592;
DT   03-SEP-1998  (first entry)
DE   Chimeric antibody against hPTRP H chain V region SEQ ID NO:57.
KW   Chimeric; antibody; human parathormone related peptide; hPTRP; mouse;
KW   L chain; H chain; hypercalcaemia; cancer; malignant lymphoma; CDR;
KW   hypophosphaemia; pathogen; vitamin D resistance; V region; C region;
KW   humanised.
OS   Synthetic.
OS   Chimeric - Mus sp.
OS   Chimeric - Homo sapiens.
PN   WO9813388-A1.
PD   02-APR-1998.
PF   24-SEP-1997; J03382.
PR   24-JUL-1997; JP-214168.
PR   26-SEP-1996; JP-255196.
PA   (CHUS ) CHUGAI SEIYAKU KK.
PI   Sato K, Wakahara Y, Yabuta N;
DR   WPI; 98-230640/20.
DR   N-PSDB; V24232.
PT   New chimeric antibodies against human parathormone related
PT   peptide(s) - useful for, e.g. treatment of hypercalcaemia and other
PT   disorders caused by malignant neoplasm(s)
PS   Claim 52; Page 120-121; 182pp; Japanese.
CC   New antibodies have been developed which are specific for human
CC   parathormone related peptides (hPTRP). The antibodies comprise chimeric
CC   L and/or H chains, where the C region is of human and L region of mouse,
CC   origin. The present sequence represents a specifically claimed region of
CC   an antibody of the invention. Host cells, transformed with vectors
CC   containing DNA encoding antibodies of the invention, can be used to
CC   produce the antibodies. The antibodies may be used to treat
CC   hypercalcaemia, especially that due to a malignancy, e.g. cancers of
CC   pancreas, lung, throat, larynx, tongue, gum, oesophagus, stomach, liver,
CC   breast, kidney, bladder, womb or prostate or malignant lymphoma. They
CC   may also be used for treatment of hypophosphaemia such as that due to
CC   pathogens or to vitamin D resistance.
SQ   Sequence   137 AA;

  Query Match           79.3%;  Score 716;  DB 1;  Length 137;
  Best Local Similarity  82.9%;  Pred. No. 1.74e-48;
  Matches   102;  Conservative    9;  Mismatches   7;  Indels   5;  Gaps   2;

Db      20 EVQLVESGGDLVKPGGSLKLSCAASGFTFSSYGMSWIRQTPDKRLEWVATISSGGSYTYY 79
           ||||||||| |||||||||||||||||:|| | |||:||||:||||||| ||||||: |||
Qy       1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60

Db      80 PDSVKGRFTISRDNAKNTLYLQMSSLKSEDTAMFYCARQTT--MTY---FAYWGQGTLVT 134
           ||:|||||||||||||||||||||||||||||||:||||::    :|   ||||||||||
Qy      61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAYWGQGTLVT 120

Db     135 VSA 137
           |||
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Qy    121 VSA 123


RESULT   14
ID   W11917 standard; Protein; 247 AA.
AC   W11917;
DT   24-JUN-1997  (first entry)
DE   Murine MAb SK48-E26 heavy chain.
KW   Interleukin-1 beta; IL-1 beta; recombinant antibody;
KW   humanised antibody; chimeric antibody; antibody engineering;
KW   monoclonal antibody; MAb; SK48-E26; inflammation; therapy.
OS   Homo sapiens.
FH   Key             Location/Qualifiers
FT   peptide         1. .19
FT                   /label= Sig_peptide
FT   region          20. .49
FT                   /label= FR1
FT                   /note= "framework region 1"
FT   region          50. .54
FT                   /label= CDR1
FT                   /note= "complementarity determining region 1
FT                   (Claim 10, page 48)"
FT   region          55. .68
FT                   /label= FR2
FT                   /note= "framework region 2"
FT   region          69. .85
FT                   /label= CDR2
FT                   /note= "complementarity determining region 2
FT                   (Claim 10, page 48)"
FT   region          86. .117
FT                   /label= FR3
FT                   /note= "framework region 3"
FT   region          118. .127
FT                   /label= CDR3
FT                   /note= "complementarity determining region 3
FT                   (Claim 10, page 48)"
FT   region          128. .138
FT                   /label= FR4
FT                   /note= "framework region 4"
FT   region          139. .247
FT                   /label= Constant_region
PN   WO9501997-A1.
PD   19-JAN-1995.
PF   07-JUL-1994; U07659.
PR   09-JUL-1993; US-090534.
PR   04-MAR-1994; US-206190.
PA   (SMIK ) SMITHKLINE BEECHAM CORP.
PI   Gross MS,  Hurle MR,  Jackson JR,  Jonak ZL,  Theisen TW;
PI   Young PR;
DR   WPI; 95-066868/09.
DR   N-PSDB; T51436.
PT   Recombinant and humanised chimeric antibodies against human
PT   interleukin-1-beta -  for preventing and treating
PT   interleukin-mediated inflammatory disorders
PS   Claim 5; Page 36-37; 62pp; English.
CC   Amino acid sequences of the heavy chain (W11917) and light chain
CC   (W11918) of anti-human interleukin-1 beta (IL-1 beta) murine
CC   monoclonal antibody (MAb) SK48-E26 were deduced form nucleic acids
CC   (T51436-37) derived from hybridoma SK48-E26.  The heavy and light
CC   chains, esp. the complementarity determining region sequences,
CC   can be utilised in novel recombinant chimeric and humanised
CC   antibodies (see also W11919-20) useful for the treatment and
CC   prevention of IL-1 mediated inflammatory disorders.
SQ   Sequence   247 AA;

  Query Match           79.3%;  Score 716;  DB 1;  Length 247;
  Best Local Similarity  84.6%;  Pred. No. 1.74e-48;
  Matches   104;  Conservative    5;  Mismatches  10;  Indels   4;  Gaps   2;

Db     20 EVHLVESGGGLVKPGGSLKLSCAASGFAFSSYDMSWVRQTPEKRLDWVAYISSGGGGTYY 79
          ||:||||||||||||||||||||||||||| |||||||||||||:|||||||||| |||
Qy      1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60

Db     80 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYHCAR-GGVRRGY---FDVWGAGTTVT 135
          |||||||||||||||||||||||||||||||||| ||| :|   :|   |  || || ||
Qy     61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAYWGQGTLVT 120

Db    136 VSS 138
          |||
Qy    121 VSA 123


RESULT   15
ID   W86122 standard; Protein; 121 AA.
AC   W86122;
DT   03-MAR-1999  (first entry)
DE   Protein sequence of de-immunised 340 Vh.
KW   Non-immunogenic; epitope; T-cell; immunogenicity; immune system; SK;
KW   immunoglobulin; therapeutic; streptokinase; de-immunised.
OS   Homo sapiens.
PN   WO9852976-A1.
PD   26-NOV-1998.
PF   21-MAY-1998; G01473.
PR   14-APR-1998; GB-007751.
PR   21-MAY-1997; GB-010480.
PR   31-JUL-1997; GB-016197.
PR   28-NOV-1997; GB-025270.
PR   02-DEC-1997; US-067235.
PA   (BIOV-) BIOVATION LTD.
PI   Carr FJ;
DR   WPI; 99-045301/04.
PT   Reducing immunogenicity of proteins - by modifying the amino acid
PT   sequence of the protein to eliminate potential epitopes for T-cells
PT   of a given species
PS   Example 1; Fig 5; 77pp; English.
CC   The invention relates to a method for the production of non-immunogenic
CC   proteins. The method comprises determining at least part of the amino
CC   acid sequence of the protein; (b) identifying in the amino acid sequence
CC   one or more potential epitopes for T-cells (T-cell epitopes) of the given
CC   species; and (c) modifying the amino acid sequence to eliminate at least
CC   one of the T-cell epitopes identified in step (b) thereby to eliminate or
CC   reduce the immunogenicity of the protein when exposed to the immune
CC   system of the given species. A method of analysing a pre-existing protein
CC   to predict the basis for immunogenic responses is also provided. The
CC   methods can be used particularly for reducing the immunogenicity of
CC   immunoglobulins or therapeutic proteins, e.g. Streptokinase (SK). The
CC   products can be used for diagnosis and therapy. The present sequence
CC   represents the protein sequence of de-immunised 340 Vh.
SQ   Sequence   121 AA;

  Query Match           79.0%;  Score 713;  DB 1;  Length 121;
  Best Local Similarity  78.9%;  Pred. No. 3.10e-48;
  Matches    97;  Conservative   10;  Mismatches  14;  Indels   2;  Gaps   1;

Db      1 EVQLVESGGGLVQPGGSLRLSCAASGFTFDTYDMSWVRQAPGKGLEWVAYIGSGGDRTYY 60
          |||||||||||| ||||:|||||||:|  |||||||:| | |||||||:||| ||
Qy      1 EVQLVESGGGLVKPGGSLKLSCAASGFAFSIYDMSWVRQTPEKRLEWVAYISSGGGTTYY 60

Db     61 PDTVKGRFTISRDNAKNTLYLQMNSLRAEDTAVYYCARHYGHYVDYAV--DYWGQGTTVT 118
          ||||||||||||||||||||:||::||||:|||||| |    |:|   |||||| ||
Qy     61 PDTVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHSGYGSSYGVLFAYWGQGTLVT 120

Db    119 VSS 121
          |||
Qy    121 VSA 123


Search completed: Mon Oct  2 09:33:25 2000
Job time : 14 secs.
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[redacted]

[redacted]

ID R84553 standard; Protein; 131 AA.
AC R84553;
DT 02-FEB-1996 (first entry)
DE MAb SCH94.03 light chain.
KW Monoclonal antibody; MAb; SCH94.03; hybridoma; central nervous system;
KW CNS; demyelination; multiple sclerosis; neural disease; therapeutic.
OS Mus sp.

FH Key	Location/Qualifiers
FT peptide	1. .20
FT	/label= Leader_peptide
FT region	44. .54
FT	/label= CDR1
FT region	70. .76
FT	/label= CDR2
FT region	109. .117
FT	/label= CDR3
FT region	116. .128
FT	/label= Joining_region
FT region	129. .131
FT	/label= C-kappa_region

PN WO9530004-A1.
PD 09-NOV-1995.
PF 27-APR-1995; U05262.
PR 29-APR-1994; US-236520.
PA (MAYO-) MAYO FOUNDATION.
PI Miller DJ, Rodriguez M;
DR WPI; 95-393077/50.
DR N-PSDB; T05311.
PT Monoclonal antibodies which stimulate central nervous system
PT re-myelination - are produced by hybridoma ATCC CRL 11627, for
PT treating multiple sclerosis, and viral or post-neural diseases of
PT the CNS.
PS Disclosure; Page 36-37; 63pp; English.
CC Hybridoma ATCC CRL 11627 was obtd. from a SJL/J mouse injected with
CC spinal cord homogenate from a mammal uninfected with any
CC demyelinating disease. The hybridoma produced a monoclonal antibody
CC (SCH94.03) useful in promoting CNS remyelination. The SCH94.03
CC light chain amino acid sequence is given in R84553.
SQ Sequence 131 AA;

Query Match 97.0%; Score 734; DB 1; Length 131;
Best Local Similarity 97.2%; Pred. No. 9.32e-50;
Matches 104; Conservative 2; Mismatches 1; Indels 0; Gaps 0;

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Db      21 DIQMTQTTSSLSASLGDRVTISCRASQDISNYLNWYQQKPDGTVKLLIYYTSRLHSGVPS 80
           ||||||||||||||||||||||||||||||||||||||||||||||||||| |||||||
Qy       1 DIQMTQTTSSLSASLGDRVTISCRASQDISNYLNWYQQKPDGTVKLLIYYTSILHSGVPS 60

Db      81 RFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPWTFGGGTKLEIK 127
           :|||||||||||||||||||:|||||||||||||||||||||||||||
Qy      61 KFSGSGSGTDYSLTISNLEQEDFATYFCQQGNTLPWTFGGGTKLEIK 107
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[redacted]